2. Non-technical Abstract

Junctional epidermolysis bullosa (EB) is one of several inherited blistering skin diseases. Children with this condition are born lacking a protein called laminin 5 β3. Without this important protein, which helps to hold skin cells together, the outermost layer of skin is easily rubbed off in blisters. Even holding these children, as any normal parent would, can result in painful sores on their skin. Ninety percent of affected children die within the first year of life, usually of severe infections or lung problems. The current treatment for this kind of EB consists of caring for the blisters. There are currently no therapies available that alter the course or severity of the disease.

We have been able to show in mice that skin cells from patients with this condition can be grown into grafts and made to produce the missing protein through gene therapy. We plan to use the same approach to make skin grafts for patients from samples of their own skin that have been re-engineered to make the missing protein. We will use these grafts to cover blisters on the patients' skin, to see if they will help the wounds heal faster and whether the grafts can keep making the missing protein laminin 5 β3 over time. In a study of 10 patients, we plan to place 2 small treated grafts to 2 sites. These grafts will be compared to two ungrafted sites, which will be treated with regular wound care. The patients will be followed at least twice a year after the first six months are completed.

This study will be one of the earliest clinical trials using gene therapy to treat skin diseases. Although there is substantial risk, we propose that its use is justified in these high risk patients who suffer from a life-threatening condition for which there are currently no other treatment alternatives that can change the course or severity of the disease.